

Autonomic Mechanisms and Therapeutic Implications of Postural Diabetic Cardiovascular Abnormalities

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Abstract

Background:

Cardiovascular autonomic neuropathy (CAN) is a disorder of progressive autonomic dysfunction (AD) associated with diabetes and other chronic diseases. Orthostatic hypotension (OH) is one of the most incapacitating symptoms of CAN and AD. AD in OH can include sympathetic withdrawal (SW). To detect and diagnose SW, parasympathetic and sympathetic changes must be clearly differentiated from each other. This is accomplished by means of the novel autonomic nervous system (ANS) method based on the simultaneous spectral analyses of respiratory activity (RA) and heart rate variability (HRV).

Methods:

We performed autonomic profiling of 184 (142 females) consecutive, arrhythmia-free patients with type 2 diabetes using the ANX-3.0 autonomic monitoring system. The patient cohort included 86 (64 female) patients for whom an α_1 -agonist was the only drug changed and increased from one test to the next; 37 (33 female) for whom the α_1 -agonist was discontinued; and 61 (45 female) who were on an α_1 -agonist, but for whom no drug changes were made. The tests averaged 3.1 ± 1.4 months apart; midodrine (ProAmatine) was the α_1 -agonist prescribed. Of the group, 99 patients also had hypertension and 47 also had cardiovascular disease. No patient had supine hypertension.

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Abbreviations: (α_1 -agonist) α_1 -adrenergic agonist, (AD) autonomic dysfunction, (ANS) autonomic nervous system, (BP) blood pressure, (CAN) cardiovascular autonomic neuropathy, (CWT) continuous wavelet transform, (DAN) diabetic autonomic neuropathy, (E/I) expiration/inspiration, (FFT) fast Fourier transform, (FRF) fundamental respiratory frequency, (HF) high frequency, (HFnu) normalized HF, (HR) heart rate, (HRV) HR variability, (LF) low frequency, (LFa) LF area, (LFnu) normalized LF, (mHR) mean HR, (OH) orthostatic hypotension, (RA) respiratory activity, (RfA) respiratory frequency area, (rHR) range HR, (RSA) respiratory sinus arrhythmia, (SB) sympathovagal balance, (SW) sympathetic withdrawal, (TSP) total spectral power

Keywords: autonomic nervous system, cardiovascular autonomic neuropathy, orthostatic hypotension, postural orthostatic tachycardia syndrome, respiratory activity analysis, vasopressor

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Abstract cont.**Results:**

Changes in parameters from the HRV (without respiration) and ANS methods were compared with changes in heart rate and blood pressure (BP) as measured from one test (test N) to the next (test $N + 1$). SW with a BP drop of less than the clinical definition may be a trend that can be an early indicator of orthostasis. In this study, patients were treated with low-dose, short-term α_1 -agonist (vasopressor) therapy, which tended to correct the abnormal trend of SW with a drop in BP. Included in the findings was a systolic BP trend in response to vasopressor therapy of an (expected) initial increase in BP followed by an eventual decrease in systolic BP as SW was reversed.

Conclusions:

The ANS method enables quantitative assessment of CAN by independently and simultaneously quantifying the two branches of the ANS, sympathetic and parasympathetic. The ANS method modifies standard spectral analysis of HRV (without RA analysis) by incorporating spectral analysis of RA.

The ANS method appears to model the normal and abnormal responses to upright posture and changes in vasopressor therapy with greater fidelity than the HRV method. Independent, simultaneous assessment of progressive parasympathetic and sympathetic dysfunction, autonomic imbalance, and responses of the two ANS branches to therapy seems to enable early detection and early intervention. Orthostasis, by way of example, illustrates that frequent, sensitive assessments of both ANS branches can improve the negative outcomes associated with CAN.

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